

IN THE SPECIFICATION:

Please amend the specification as follows:

At page 6, please replace the paragraph beginning “Figure 3A) Maximal average sequence” with the following amended paragraph:

Figure 3A) Maximal average sequence identity of cross-reactive proteins for antibodies targeted against Tpk1p. 3B) Maximal average sequence identity of cross-reactive proteins for antibodies targeted against CDC11p. 3C) Maximal average sequence identity of cross-reactive proteins for antibodies targeted against Rud3p. x-axis = sequence window number, y-axis = maximal average identity. Methods as described in text. Regions of maximal similarity are indicated by arrows. 3D) Sequence alignment of and around the immunogenic peptide region with best matches from each of the cross reacting peptides: Hda1 (SEQ ID NO:42); YMR004W (SEQ ID NO:43); MJR056C (SEQ ID NO:44); YMR110C (SEQ ID NO:45); YLR332W (SEQ ID NO:46); YNR034W (SEQ ID NO:47); YDL204W (SEQ ID NO:48); YDR510W (SEQ ID NO:49); and YDR469W (SEQ ID NO:50). The immunogenic peptide is underlined in the Hda1 sequence. The 8 amino acid window with highest maximal sequence identity between all cross-reacting proteins is depicted in bold.

At page 48, please replace the paragraph beginning “The analysis was followed up” with the following amended paragraph:

The analysis was followed up for the antibody targeted against Hda1, for which it was determined the antibody was raised against a 21 amino acid peptide with the sequence TDGLNNIIEERFEEATDFILD (SEQ ID NO:17). Comparison of this sequence with the sequence cross comparison of the 7 reactive proteins shows that the region of highest similarity (see Figure 3C) is entirely contained within the 21 amino acid sequence of the peptide (Figure 3D). To confirm this peptide as a common epitope on the proteins that cross-react with the anti-Hda1 antibody, arrays were probed with the antibody in the presence of an excess amount of the immunizing peptide; a peptide of similar length but different sequence was used as a control. As shown in Figure 2C, the Hda1 blocking peptide inhibits the interaction of anti-Hda1 with its cognate antigen Ynl021W-Hda1 as well to each of the seven cross-reacting proteins. No inhibition of anti-Hda1 binding to these proteins was observed with the control peptide.

At page 53, please replace the paragraph beginning “**Amino Acid Composition of Hda1 blocking peptide**” with the following amended paragraph:

Amino Acid Composition of Hda1 blocking peptide. Anti-Hda1 blocking peptide was purchased from Santa Cruz Biotechnologies, Inc (Santa Cruz, CA; 0.2ug/ul in 1XPBS). Peptide was analyzed for amino acid composition using a Beckman 7300 amino acid analyzer at the HHMI Biopolymer Keck Foundation Bioresearch Laboratory at Yale University. Comparison of the amino acid composition with the linear sequence of Hda1 was used to determine the peptide sequence: TDGLNNIIEERFEEATDFILD (SEQ ID NO:17).

At page 56, please replace the paragraph beginning “In order to assess the utility of sequence” with the following amended paragraph:

In order to assess the utility of sequence analysis in predicting cross reactivity, all yeast proteins were searched for either the 8 amino acid epitope core sequence NNIEERF (SEQ ID NO:1) or the 20/21 amino acid immunogenic peptide sequence TDGLNNIIEERFEEATDFILD (SEQ ID NO:17). The top matches are presented in Table 4. In addition to the observed cross-reactive proteins, a large number of proteins are identified with similarly high sequence conservation which show no empirical evidence of cross reactivity. Thus, although sequence analysis is useful in explaining the observed cross-reactivity, it is clearly insufficient to predict it.

At page 56, please replace **Table 2** with the following amended Table (insertions are indicated by double underscoring):

Table 2. Sequence alignments for the 3 regions of highest homology based on a comprehensive 8 amino acid window sequence comparison. Sequence alignment is shown for 12 amino acids – the 8 amino acid core (bold in all, underlined for reference sequence YNL021W) and 2 amino acids on both N’ and C’. Identities are in red.

<u>Sequence</u>	<u>SEQ ID NO.</u>	<u>Protein</u>	<u>Identity (in 8 aa core)</u>
Region 1			
EEENSLSTTSKS	<u>SEQ ID NO:2</u>	YNL021W	
ESEESSSTNSVI	<u>SEQ ID NO:3</u>	YDR469W	.625
EQADSSSLTSFS	<u>SEQ ID NO:4</u>	YLR332W	.5
VMENLLTTAGVS	<u>SEQ ID NO:5</u>	YMR110C	.5
TDEGSYSTSIKS	<u>SEQ ID NO:6</u>	YDL204W	.5
Region 2			
FNEPINDSIISK	<u>SEQ ID NO:7</u>	YNL021W	
GGEPINSSVASN	<u>SEQ ID NO:8</u>	YLR332W	.625
KNEPYIDKIISK	<u>SEQ ID NO:9</u>	YDL204W	.625
FNETINKIIESK	<u>SEQ ID NO:10</u>	YMR110C	.5
MNYLIEQSNILK	<u>SEQ ID NO:11</u>	YDR469W	.375
Region 3			
GLNNIIEERFEE	<u>SEQ ID NO:12</u>	YNL021W	
ASNDIIEEKFYD	<u>SEQ ID NO:13</u>	YLR332W	.75
TINKIIEEHDTF	<u>SEQ ID NO:14</u>	YMR110C	.625
NQNVKIEESSEP	<u>SEQ ID NO:15</u>	YDR469W	.5
NLFNNRHENFDE	<u>SEQ ID NO:16</u>	YDL204W	.375

At page 57, please replace “**Table 3.** Sequence alignment of the immunogenic” with the following amended Table (insertions are indicated by double underscoring):

Table 3. Sequence alignment of the immunogenic peptide region with best matches from each of the 4 ‘cross-reactive’ proteins. The 8 amino acid core from region 3 (Figure 1) is in bold for all sequences, and underlined in the reference sequence

<u>Sequence</u>	<u>SEQ ID NO.</u>	<u>Protein</u>
TDGLNNIIEERFEEATDFILD	<u>SEQ ID NO:17</u>	YNL021W
SVASNDIIEEKFYDEQGNELS	<u>SEQ ID NO:18</u>	YLR332W
KDFHRNKIESVLNETTKLMND	<u>SEQ ID NO:19</u>	YMR110C
FHKNYNKVVEKTEPYIDKIIP	<u>SEQ ID NO:20</u>	YDL204W
SSSTNSVIEESSEPKISKLEN	<u>SEQ ID NO:21</u>	YDR469W

At page 57, please replace “**Table 4.**” with the following amended Table (insertions are indicated by double underscoring):

Table 4.

<u>Sequence</u>	<u>SEQ ID NO.</u>	<u>Protein</u>	<u>Identity</u>
TDGLNNIIEERFEEATDFILD	<u>SEQ ID NO:22</u>	YNL021W	1.000
TNGRNIIIEEIEASRTSFTLY	<u>SEQ ID NO:23</u>	YDR291W	0.476
TDYLKNIIVENSGTSGDEDVD	<u>SEQ ID NO:24</u>	YIL075C	0.429
RDYLN SYIEERLQEEHLDINN	<u>SEQ ID NO:25</u>	YKL201C	0.429
KTDLVNFIEERFKTFCDEELE	<u>SEQ ID NO:26</u>	YKR054C	0.429
TVLENKKIEEGKETAVDREED	<u>SEQ ID NO:27</u>	YKL188C	0.429
IEGLNISSGTFESLQDFVLQ	<u>SEQ ID NO:28</u>	YNL193W	0.429
TDASNGYDEELPEEEQEFSDD	<u>SEQ ID NO:29</u>	YNL124W	0.429
SYYLNCIIEENFKEMTRKLQR	<u>SEQ ID NO:30</u>	YNL126W	0.429
GQFLENFLELNLNEVTDLIRD	<u>SEQ ID NO:31</u>	YDR481C	0.381
TLSAGNACPGWDEDANDDILD	<u>SEQ ID NO:32</u>	YBR092C	0.381
TDIFKNCLNQFEITNLKILF	<u>SEQ ID NO:33</u>	YKL057C	0.381
DDDDDDDEDEEEEEVTDQLED	<u>SEQ ID NO:34</u>	YFR033C	0.381
VDGKGNETEEDDIKFIKGILD	<u>SEQ ID NO:35</u>	YJL168C	0.381
DDGLPNGITLIGKKFTDYALL	<u>SEQ ID NO:36</u>	YBR208C	0.381
TISLIHEIEKIFEEDIHFEQN	<u>SEQ ID NO:37</u>	YHR184W	0.381
FQGGLDIIKESLEEDPDLQH	<u>SEQ ID NO:38</u>	YDR098C	0.381
TDYLFDYREVLESLGLDIILD	<u>SEQ ID NO:39</u>	YLR443W	0.381
QFLLSKIIEARISGAFFEIWD	<u>SEQ ID NO:40</u>	YDL231C	0.381
TEFYNNYSMQVREDERDYILD	<u>SEQ ID NO:41</u>	YDL040	0.381

Please amend the specification by entering the Sequence Listing that is being submitted concurrently herewith.